## Remarks

The Office Action mailed March 28, 2007, has been received and reviewed. Claims 1, 3-5, 10-12, 30, and 32-37 having been amended, claims 8 and 14-29 having been canceled, without prejudice, and claims 38 and 39 having been added, the pending claims are claims 1-7, 9-13, and 30-39. Claims 32, 34, 35, and 37 being withdrawn from examination as drawn to non-elected inventions, claims 1-7, 9-13, 30, 31, 33, and 36 are currently under examination. Reconsideration and withdrawal of the rejections are respectfully requested.

Support for the claims amendments is found throughout the specification. For example, support for the recitation "'wherein the at least one additional therapeutic agent is a cytotoxic antineoplastic chemotherapy agent" in amended claim 1 and the recitation "cytotoxic antineoplastic chemotherapy agent" in amended claims 32-34 is found, for example, in original claim 3, page 2, lines 20-21, and page 46, lines 28-29 of the specification. Support for the recitation "wherein the at least one additional therapeutic agent is previously known to be therapeutically effective for the treatment of said cancer" in amended claim 3 is found, for example, on page 15, lines 9-12 of the specification.

The Examiner requested clarification as to the status of claims 10-23. Page 4 of the Preliminary Amendment filed January 19, 2007, inadvertently indicated that the status of claims 10-23 was "cancelled." Applicants apologize for this typographical error. As indicated in the present Amendment and Response, claims 10-13 are pending and claims 14-29 have been cancelled.

## Oath/Declaration

The Examiner expressed concern that the Declaration executed by Andrew Mellor on June 16, 2004 was defective, as corrections were not initialed and dated. Submitted herewith is a replacement Declaration executed by Andrew Mellor on September 24, 2007.

## Priority

The Examiner asserted (bridging pages 3-4, Office Action mailed March 28, 2007) that U.S. Provisional Application Nos. 60/459,489 and 60/538, 647 "are drawn to methods using D-isomer inhibitors of indoleamine-2,3-dioxygenase. There is no support in said application for methods of administering inhibitors of indoleamine-2,3-dioxygenase generally. As such, only claims 10-12 are entitled to benefit of the earlier filed applications. Claims 1-9, 13-34, 19 and 24-37 are afforded an effective filing date of 2/17/2004 (filing date of instant application). Claims 10-12 are afforded an effective filing date of 4/1/2003 (filing date of the '489 application)" (page 4, Office Action mailed March 28, 2007 (emphasis in original)).

Applicants adamantly, yet respectfully disagree. Applicants submit that U.S. Provisional Application No. 60/459,489, filed April 1, 2003, provides ample support for methods of administering inhibitors of indoleamine-2,3-dioxygenase generally. For example, Applicants direct the Examiner to Example 2 (see, for example, page 33, line 26 to page 34, line 11) and Figure 7 of U.S. Provisional Application No. 60/459,489, filed April 1, 2003, demonstrating the "inhibition of tumor growth by DL-racemic mixtures of 1-MT" and to page 8, line 20, page 12, line 30 to page 13, line 6 and page 31, lines 22-26 U.S. Provisional Application No. 60/459,489, which further discuss inhibitors of indoleamine-2,3-dioxygenase other than D isomers of inhibitors of indoleamine-2,3-dioxygenase.

Applicants respectfully insist that the record be corrected to indicate that the Examiner's statement concerning the priority of the present application is incorrect.

## Restriction Requirement

Applicants thank the Examiner for the rejoinder of claims 19, 24-31, and 36 with Group I. Applicants continue to request the rejoinder of Group III (amended claims 32 and 34) and Group IV (amended claims 35 and 37) with elected Group I. As amended, Applicants

submit that the burden to search and examine the methods of Groups III and IV along with Group I is not unduly burdensome. Rejoinder and examination of the claims of Groups III and IV along with the claims of I is respectfully requested.

In maintaining the restriction requirement, the Examiner asserted that "claims drawn to 'augmenting the rejection of tumor cells' and 'reducing tumor size or slowing tumor growth' are distinct from methods of treating cancer. The methods of treating cancer as instantly claimed require . . . that the subject have cancer. However, claims drawn to methods of augmenting tumor rejection or reducing tumor size are not limited to malignant tumors. As such, the search required for these methods is broader than that required for cancer" (page 2, Office Action mailed march 28, 2007). Applicants respectfully disagree and direct the Examiner to page 17, lines 21-20 of the specification, which states, "[a]s used herein, 'tumor' refers to all types of cancer, neoplasm, or malignant tumors found in mammals." Further, '[t]he efficacy of treatment of a tumor may be assessed by any of various parameters well known in the art. This includes, but is not limited to, determinations of a reduction in tumor size, [and] determinations of the inhibition of growth" (page 17, lines 23-27 of the specification).

Further, Applicants submit that while the method of Group I and the methods of Group III and IV have different preambles, the methods of Groups I, III, and IV all have the same active step, all drawn to methods "comprising administering to the subject an inhibitor of indoleamine-2,3-dioxygenase in an amount effective to reverse indoleamine-2,3-dioxygenase-mediated immunosuppression, and administering at least one additional therapeutic agent."

Rejoinder and examination of the claims of Groups III and IV along with the claims of I is respectfully requested.

**Double Patenting Rejection**

Claims 1-14, 19, 24-31, 33, and 36 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 6-10 and 17-

26 of co-pending U.S. Patent Application Serial No. 10/780,150. This provisional rejection is traversed.

Instant claims 1-14, 19, 24-31, 33, and 36 are drawn to *"methods of treating cancer."* Claims 6-10 and 17-26 of co-pending U.S. Patent Application Serial No. 10/780,150 all depend from independent claim 42 and are drawn to a "*method of delaying the relapse or progression of a tumor in a subject.*"

In the present application, in a Restriction Requirement mailed December 20, 2006, the Examiner restricted claims drawn to *"methods of treating cancer"* into restriction Group I, while claims drawn to "*methods of augmenting the rejection of tumor cells"* (claims 32 and 35) and *"methods of reducing tumor size of slowing tumor growth in a subject"* (claims 34 and 37) were restricted into Groups III and IV. In maintaining the restriction requirement between Group I and Groups III and IV, the Examiner asserted that "claims drawn to 'augmenting the rejection of tumor cells' and 'reducing tumor size or slowing tumor growth' are distinct from methods of treating cancer. The methods of treating cancer as instantly claimed require . . . that the subject have cancer. However, claims drawn to methods of augmenting tumor rejection or reducing tumor size are not limited to malignant tumors. As such, the search required for these methods is broader than that required for cancer" (page 2, Office Action mailed march 28, 2007).

Applicants respectfully submit that the Examiner has placed claims drawn to methods of treating cancer and claims drawn to methods of altering tumor growth into separate restriction groups. If this restriction requirement is maintained, Applicants respectfully remind the Examiner that it is inappropriate to reject claims on the ground of nonstatutory obviousness-type double patenting when the U.S. Patent Office has issued a Restriction Requirement restricting the claims of the present application and the claims of the co-pending application into different restriction groups. Reconsideration and withdrawal of this provisional rejection of claims 1-7, 9-13, 30, 31, 33 and 36 on the ground of nonstatutory obviousness-type double patenting as being

unpatentable over claims 6-10 and 17-26 of co-pending U.S. Patent Application Serial No. 10/780,150 is requested.

**The 35 U.S.C. §112, Second Paragraph, Rejection**

The Examiner rejected claims 1-2, 8-14, 19, and 28 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. This rejection is traversed.

Specifically, the Examiner asserted that the recitation "one additional therapeutic agent" in claims 1-2 and 8-14 "is indefinite because it is not clear what the agent is therapeutically effective for" (page 10 of Office Action mailed March 28, 2007). Applicants submit that this rejection is overcome in view of the amendment clarifying claim 1 to recite "wherein the at least one additional therapeutic agent is a cytotoxic antineoplastic chemotherapy agent."

Further, the Examiner asserted that the recitation "vaccine" in claims 19 and 28 is indefinite. Applicants respectfully disagree, submitting that "vaccine" is a well understood term of art. However, to expedite prosecution, claims 19 and 28 have been canceled. Applicants reserve the right to continue the prosecution of cancelled subject matter in related applications. Applicants submit that this rejection is moot in view of the cancellation of claims 19 and 28.

Reconsideration and withdrawal of the rejection of 1-2 and 9-13 under 35 U.S.C. §112, second paragraph, is requested.

**The 35 U.S.C. §102 Rejection**

The Examiner rejected claims 1, 9, 13 and 30-31 under 35 U.S.C. §102 as being anticipated by WO 00/66764. This rejection is traversed. According to MPEP § 2131 a "claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference."

Amended independent claim 1 (and dependent claims 9, 13, 30, and 31) are drawn to methods "of treating a subject with a cancer, the method comprising administering to the subject an inhibitor of indoleamine-2,3-dioxygenase in an amount effective to reverse indoleamine-2,3-dioxygenase-mediated immunosuppression, and administering at least one additional therapeutic agent, *wherein the administration of the inhibitor of indoleamine-2,3-dioxygenase and the at least one additional therapeutic agent demonstrate therapeutic synergy, wherein at least one additional therapeutic agent is a cytotoxic antineoplastic chemotherapy agent,* and wherein the inhibitor of indoleamine-2,3-dioxygenase is selected from the group consisting of 1-methyl-tryptophan, β-(3-benzofuranyl)-alanine, β-(3-benzo(b)thienyl)-alanine, and 6-nitro-D-tryptophan."

WO 00/66764 teaches administering tryptophan enhancing agents, such as 1-methyl-tryptophan, to increase T cell proliferation *in vitro* and *in vivo*, to treat disorders characterized by constitutive expression of IDO, and for the treatment of cancer (see, for example, abstract, claims 8 and 9, page 2, lines 4-8 and 12-14, page 3, lines 30-34, and page 6, lines 17-25). WO 00/66764 also teaches administering tryptophan enhancing agents, such as 1-methyl-tryptophan, along with other agents, such as "T cells, antigens (e.g., peptides, proteins), nucleic acids encoding antigens . . . which stimulate an immune response" (page 16, lines 22-30 of WO 00/66764 ). Further, other agents that stimulate an immune response, such as cytokines, can also be administered along with tryptophan enhancing agents (page 17, lines 11-18 of WO 00/66764). Thus, the teachings of WO 00/66764 are limited to the administration other *agents that stimulate an immune response* along with the administration of a tryptophan enhancing agent.

WO 00/66764 does not teach methods "comprising administering to the subject an inhibitor of indoleamine-2,3-dioxygenase in an amount effective to reverse indoleamine-2,3-dioxygenase-mediated immunosuppression, *and administering at least one additional therapeutic agent, wherein the administration of the inhibitor of indoleamine-2,3-dioxygenase and the at least one additional therapeutic agent demonstrate therapeutic synergy, wherein at*

*least one additional therapeutic agent is a cytotoxic antineoplastic chemotherapy agent.*" Thus, the disclosure of WO 00/66764 does not set forth each and every element of claims 1, 9, 13, 30, and 31. Withdrawal of this rejection under 35 U.S.C. §102(b) is respectfully requested.

**The 35 U.S.C. §112, First Paragraph, Written Description Rejection**

Claims 1-7, 13, 30, 31, 33 and 36 were rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. This rejection is traversed.

The Examiner rejected claims 1-7, 13, 30, 31, 33, and 36, asserting that the specification fails to provide adequate written description for the recitation "an inhibitor of indoleamine-2,3-dioxygenase" (page 5, Office Action mailed March 28, 2007). Applicants respectfully disagree. "To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention" (MPEP § 2163). Generally, "there is an inverse correlation between the level of skill and knowledge in the art and the specificity of disclosure necessary to satisfy the written description requirement. Information which is well known in the art need not be described in detail in the specification." See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1379-80, 231 USPQ 81, 90 (Fed. Cir. 1986). Applicants submit that "compounds that serve as . . . inhibitors of the IDO enzyme are . . . well known" (page 14, lines 28 of the specification) to those of skill in the art. See, for example, the lengthy description of inhibitors of indoleamine-2,3-dioxygenase listing in WO 00/66764 (page 6, line 21 to page 12, line 32). However, to expedite prosecution, claims 1, 5, 33, and 26 have been amended to recite "wherein the inhibitor of indoleamine-2,3-dioxygenase is selected from the group consisting of 1-methyl-tryptophan, β-(3-benzofuranyl)-alanine, β-(3-benzo(b)thienyl)-alanine, and 6-nitro-D-tryptophan." Applicant reserve the right to continue the prosecution of canceled subject matter in related applications.

Applicants submit that rejections of claims 19, 24, 26, and 28 are moot in view of the cancellation of these claims. Applicant reserve the right to continue the prosecution of canceled subject matter in related applications.

Reconsideration and withdrawal of the rejection of claims 1-7, 13-14, 19, 24-31, 33 and 36 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement, is requested.

**The 35 U.S.C. §112, First Paragraph, Enablement Rejection**

The Examiner rejected claims 1-7, 9-13, 30, 31, 33, and 36 under 35 U.S.C. §112, first paragraph, alleging the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claims. Specifically, the Examiner asserted that the specification "does not reasonably provide enablement for the treatment of *all cancers* by administering *any inhibitor of indolemanine-2,3 dioxygenase* combined with *any chemotherapeutic agent* (page 13, Office Action mailed March 28, 2007). Applicants respectfully submit that this rejection is moot in view of the amendments to the claims.

As amended, independent claims 1 and 33 (and dependent claims 2-4, 9, 11, 13, 30 and 31) are draw to methods of treating a subject with a cancer comprising administering an inhibitor of indoleamine-2,3-dioxygenase (IDO) selected from the group consisting of 1-methyl-tryptophan, β-(3-benzofuranyl)-alanine, β-(3-benzo(b)thienyl)-alanine, and 6-nitro-D-tryptophan and administering at least one additional cytotoxic antineoplastic chemotherapy agent. And, as amended, independent claims 5 and 36 (and dependent claims 6, 7, 10, and 12) are drawn to methods of treating a subject with a cancer comprising administering an inhibitor of indoleamine-2,3-dioxygenase selected from the group consisting of 1-methyl-tryptophan, β-(3-benzofuranyl)-alanine, β-(3-benzo(b)thienyl)-alanine, and 6-nitro-D-tryptophan and

administering radiation therapy. Applicants submit that the specification is fully enabling for the claimed methods.

"The immune system of a tumor-bearing host often fails to respond protectively against tumor antigens. Functionally, the host is tolerant toward the tumor" (page 1, lines 30-31 of the specification). "This tolerance allows tumors to escape the host's normal immune surveillance and imposes a fundamental barrier to successful clinical immunotherapy" (page 2, lines 7-9 of the specification). Example 2 of the specification demonstrates that immune cells (plasmacytoid dendritic cells (DCs)) in tumor-draining lymph nodes mediate this immunosuppression via indoleamine 2,3-dioxygenase (IDO) and that this immunosuppression can be abrogated by the administration of an inhibitor of IDO, indicating "that the IDO-expressing DCs create a local microenvironment in tumor-draining lymph nodes that suppresses host anti-tumor cytotoxic T cell responses" (see, for example, page 32, lines 1-3, and 10-13 of the specification).

Thus, tumors actively create a state of tolerance toward their own antigens, allowing tumors to escape from host immune surveillance and imposing barriers to effective anti-tumor immunotherapy. With the present invention, the administration of an IDO inhibitor prevents such IDO-mediated immunosuppression; "the administration of an inhibitor of indoleamine-2,3-dioxygenase to a subject suffering from a tumor . . . in combination with administration of an additional therapeutic agent results in an improved efficacy of therapeutic outcome" (page 13, lines 20-28 of the specification). For example, Example 3 of the specification demonstrates that the administration of an 1-MT to tumor-bearing hosts in conjunction with low-dose chemotherapy (cyclophosphamide) or radiation shows synergistic immune-mediated anti-tumor effect (page 46, lines 18-20 of the specification).

Cytotoxic antineoplastic chemotherapy agents and radiation (both widely used in human cancer therapies) release large amounts of antigen from dying tumor cells, but, because of IDO-mediated immunosuppression, these tumor antigens do not normally generate a useful

immune response. With the methods of the present invention, the coadministration of an inhibitor of IDO prevents such IDO-mediated immunosuppression, thus allowing a vigorous immune response to the tumor (page 46, lines 28-30 of the specification). The administration of a cytotoxic antineoplastic agent or radiation along with an IDO inhibitor is more effective than the administration of any these agents in the absence of an IDO inhibitor because both cytotoxic antineoplastic agents and radiation induce tumor cell damage and release of large amounts of tumor associated agents, against which an immune response can be mounted. In the absence of an IDO inhibitor, immune stimulation to such tumor antigen exposure is quenched by IDO+ DCs in the tumor draining lymph node, resulting in the induction of immunotolerance to the tumor antigens.

Applicants submit that the specification is fully enabling for the claimed methods, methods of treating a subject with a cancer comprising administering an inhibitor of indoleamine-2,3-dioxygenase (IDO) selected from the group consisting of 1-methyl-tryptophan, β-(3-benzofuranyl)-alanine, β-(3-benzo(b)thienyl)-alanine, and 6-nitro-D-tryptophan and administering at least one additional cytotoxic antineoplastic chemotherapy agent (claims 1-4, 9, 11, 13, 30, 31, and 33) and methods of treating a subject with a cancer comprising administering an inhibitor of indoleamine-2,3-dioxygenase selected from the group consisting of 1-methyl-tryptophan, β-(3-benzofuranyl)-alanine, β-(3-benzo(b)thienyl)-alanine, and 6-nitro-D-tryptophan and administering radiation therapy (claims 5, 6, 7, 10, 12, and 36).

Applicants submit that several peer-reviewed publications support the effectiveness of the claimed methods, administering a variety of IDO inhibitors and cytotoxic antineoplastic agents in the treatment of a variety of cancers. Specifically, Applicants direct the Examiner to Muller et al., *Expert Opin Ther Tagets* (2005) 9(4):831-849) (PTO-892 mailed March 28, 2007); Muller et al., *Nat Med* (2005) 11(3):312-319) (PTO-1449 submitted herewith); and Hou et al., *Cancer Res* (2007) 67(2):792-801) (PTO-1449 submitted herewith). In MMTV-*Neu* mice, a well-accepted transgenic mouse model of breast cancer, 1MT administered along with a variety

of cytotoxic chemotherapeutic drugs (paclitaxel, cisplatin, cyclophosphamide, doxorubicin, and farnesyltransferase inhibitor (FTI)) exhibits enhanced anti-tumor activity (see pages 835-36 of Muller et al., *Expert Opin Ther Targets* (2005); pages 315-316, Fig. 1 and Table 1 of Muller et al., *Nat Med* (2005); and page 794 of Hou et al. Hou et al. demonstrates the synergistic antitumor effect of 1MT administered along with gemcitabane (see Fig 5A and page 797) in the B16F10 melonoma tumor system and confirms the synergistic antitumor effect of 1MT administered with cyclophosphamide or radiation in the B16F10 melonoma tumor system previously demonstrated by the present specification (see Figs. 1A-C and 5A and pages 793 and 797 of Hou et al.). Further, Hou et al. demonstrates the synergistic antitumor effect of 1MT administered along with cyclophosphamide in the 4T1 tumor model system of breast cancer (see Figs. 2A and 6A and page 794 of Hou et al.).

Citing Muller et al., *Expert Opin Ther Targets* (2005) 9(4):831-849, the Examiner asserted "it is clear that not all chemotherapeutic agents will be 'cooperative' with inhibition of indoleamine-2,3-dioxygenase in the treatment of cancer" (page 16 of Office Action mailed March 28, 2007). Applicants submit that the claimed methods are not drawn to the administration of "all chemotherapeutic agents," but rather to "cytotoxic antineoplastic agents." Muller states that "IDO inhibitors can cooperate with cytotoxic agents to more effectively destroy tumors" (see page 831) and "[w]hat was perhaps counterintuitive, however, was the finding that standard cytotoxic chemotherapeutic agents show striking cooperativity" (see bottom of column 2, page 843). Further, as discussed above, Muller demonstrates cooperativity of IDO inhibitors with the cytotoxic antineoplastic agents paclitaxel, cisplatin, cyclophosphamide, doxorubicin, and farnesyltransferase (see page 835) and demonstrates effectiveness in an additional animal model of cancer (the well-accepted MMTV-Neu 'oncomouse' model of breast cancer) (see page 835). Finally, Muller et al. Discusses a wide variety of IDO inhibitors (see pages 836-842). Thus, Applicants submit that the teachings of Muller et al. support the enablement of the present claims.

Illustrative of the state of the art in the treatment of cancer, the Examiner cites Gura et al. (*Science* 1997, 278:1041-1042) and Johnson et al., (*British J. Cancer* 2001, 84(10):1424-1431) (pages 15-16 of Office Action mailed March 28, 2007). The present application has a priority date of April 1, 2003. Applicants submit that publications published in 1997 (Gura et al.) and 2001 (Johnson et al.) cannot properly represent the state of the art at the time of the filing of the present application (2003) in rapidly advancing fields such as immunology and the treatment of cancer. Further, Applicants submit that the teachings of Gura et al. and Johnson et al. have no relevance to the present invention. As acknowledged by the Examiner, both Gura et al. and Johnson et al. pertain to the screening of candidate compounds for the identification of new agents that are effective for the treatment of cancer. The present claims are drawn to treating cancer by administering already available cytotoxic antineoplastic chemotherapy agents (independent claims 1and 33) or radiation therapy, which is already known for its effectiveness in treating cancer (independent claims 5 and 36). Issues associated with identifying new candidate agents for the treatment of cancer have no relevance to the presently claimed methods, all of which include the administration of agents already available for the treatment of cancer.

Further, the Examiner asserted that, as the specification "states that 1-methyl-tryptophan is not an efficient inhibitor of indoleamine-2,3-dioxygenase (page 29, line 22) and a racemic mixture is only partially effective in reversing IDO-mediated inhibition of T cell proliferation (*id.* at lines 23-24) . . . it appears that stereochemistry may play an important role in a compound's ability to inhibit indoleamine-2,3-dioxygenase and that even inhibitors of indoleamine-2,3-dioxygenase are not always effective in reversing IDO-mediated inhibition of T cell proliferation" (page 18 of Office Action mailed March 28, 2007). Applicants respectfully submit that this assertion is a misinterpretation of the teachings of the specification. While the specification observes that "the D-isomer of 1-MT . . . gave better reversal of suppression with less toxicity than the DL-racemic mixture used previously," "1MT is not an efficient inhibitor of IDO (Km of approximately 30 μM)," "[w]hen the number of IDO+ DCs is large, a racemic

mixture of 1MT is only partially effective in reversing IDO-mediated inhibition of T cell proliferation," and "this reflects the less-than-perfect efficiency of a racemic mixture of IMT as an inhibitor of IDO" (see page 29 lines 19-29 of specification), these observations do not substantiate the Examiner's conclusion that inhibitors of indoleamine-2,3-dioxygenase are not always effective in reversing IDO-mediated inhibition of T cell proliferation. While the D isomer of 1MT may be more effective (page 47, lines 6-7 and page 49, lines 9-11 of the specification), both a racemic mixture and the L isomer of 1 MT demonstrate efficacy in reversing IDO-mediated suppression (see, for example, Figures 10 and 11 and page 11, line 24 to page 12, line 5 of the specification and page 48, line 26 to page 49, line 15 of the specification).

In view of the above discussion, reconsideration and withdrawal of this rejection of claims 1-14, 19, 24-31, 33, and 36 under 35 U.S.C. §112, first paragraph, as not enabled by the specification is requested.

## Summary

It is respectfully submitted that the pending claims 1-7, 9-13, and 30-39 are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

CERTIFICATE UNDER 37 C.F.R. 1.10:

The undersigned hereby certifies that this paper is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR §1.10 on the date indicated below and is addressed to Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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